REMARKS

Reconsideration and withdrawal of the rejections set forth in the Office action dated September 14, 2010 are respectfully requested. Claims 1-6 are pending and claims 7-14 are withdrawn.

I. Amendments

Claim 1 is amended to clarify that the expression vector comprises nucleic acid sequences encoding the recited polypeptide sequences. Claim 1 is further amended to recite the step of displaying the anchor tethered protein on a lipid bilayer array or purifying and reconstituting the anchor tethered protein in membranes for display on a lipid bilayer array. Basis for these amendments can be found, for example, on page 6, lines 28-32 and in Examples 4-5 on pages 19-20 .

Claim 2 is amended to recite glycosylphosphatidylinositol as the entire phrase for the abbreviation GPI as stated on page 2, line 8.

Claim 3 is amended to recite the sequence identifier.

Claim 4 is amended to recite Chinese hamster ovary as the entire phrase for the abbreviation CHO as stated on page 11, line 21.

Claim 5 is amended to clarify that the signal sequence is an epidermal growth factor signal sequence. Basis for this amendment can be found, for example, on page 10, lines 3-5.

No new matter is added by way of these amendments.

II. Objections to the Specification

The specification was objected to for containing an embedded hyperlink and/or other form of browser-executable code. Applicants have amended the specification to remove the "www" portion of the website addresses recited in the specification. Accordingly, Applicants respectfully request withdrawal of the objections to the specification.

III. Claim Objections

Claims 2-3 were objected to because of the following informalities:

(a) Claim 2 recites the abbreviation "GPI". Applicants have amended the claim to recite glycosylphosphatidylinositol.

(b) Claim 3 recites "the 32 terminal amino acids ... ". Applicants have amended claim 3 to reference the sequence identifier.

(c) Claim 4 recites the abbreviation "CHO". Applicants have amended the claim to recite Chinese hamster ovary.

In view of the above, Applicants respectfully request withdrawal of the objections to the claims.

IV. Rejections Under 35 U.S.C. § 112, second paragraph

Claims 1-6 were rejected under of 35 U.S.C. § 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 was rejected as allegedly indefinite for the language "5' signal sequence", "a purification epitope tag...a 3' anchor sequence". Specifically the Examiner notes that an expression vector consists of nucleic acids that encode polypeptides having the recited functions. Accordingly, Applicants have amended claim 1 in accord with the Examiner's kind suggestions.

Claim 1 was further rejected for the language "the extracellular domain" as allegedly lacking antecedent basis. Applicants note that the preamble introduces the feature of extracellular domains. However, Applicants have amended claim 1 to reference "an extracellular domain" to enhance clarity.

Claim 3 was rejected for the language "the 32 terminal amino acids of the GPI-anchoring sequence" as allegedly lacking antecedent basis. The amendments to claim 3 obviate this rejection.

In view of the above, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

V. Claim Rejections Under 35 U.S.C. § 112, first paragraph

Claims 1-6 were rejected under 35 U.S.C. § 112, first paragraph, written description, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that

the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-6 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for a method for generating tethered extracellular domains of transmembrane protein by preparing an expression vector having a known signal sequence at 5'; allegedly does not reasonably provide enablement for method of preparing an expression vector having any epidermal growth factor sequence encoding nucleic acid as a signal sequence at 5' for generating tethered extracellular domains of transmembrane protein.

A. Written Description

The Examiner asserts that the specification fails to provide an adequate written description for an epidermal growth factor having a function as a signaling peptide (Office action , page 7-8). Applicants have amended claim 5 to clarify that the signal sequence is an epidermal growth factor "signal sequence". Thus, claim 5 encompasses a method of using an epidermal growth factor signal sequence as the signal sequence.

The essential purpose of the written description requirement is to show the possession of the invention as of the filing date as a *prima facie* date of invention. *In re Smith*, 481 F.2d 910, 178 U.S.P.Q. 620, 623 (CCPA 1973). Accordingly, the specification is required to contain a statement that adequately describes the invention as claimed. Applicants direct the Examiner to page 9, line 34 to page 10, line 5, for example where it is clear that Applicants had possession of a method using the signal sequence of epidermal growth factor.

In view of the above, one skilled in the art would reasonably conclude that Applicants were in possession of the claimed invention at the time the invention was filed. Withdrawal of the rejection of the claims under 35 U.S.C. §112, first paragraph as allegedly containing subject matter which was not described in the specification at the time of filing is respectfully requested.

B. Enablement

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. That some experimentation may be required

is not fatal; the issue is whether the amount of experimentation is undue (see, for example, *In re Vaeck*, 20 USPQ 1438 (Fed. Cir. 1991).

The Examiner acquiesces that the specification enables "a method for generating tethered extracellular domains of transmembrane protein by preparing an expression vector having a known signal sequence at 5'" (Office action page 8). The Examiner asserts, however, that the specification does not reasonably provide enablement for a method of preparing an expression vector having any epidermal growth factor sequence encoding nucleic acid *as a signal sequence*. Applicants have amended claim 5 to clarify that the signal sequence is an epidermal growth factor *signal sequence*. In light of the amendments to the claims, Applicants submit that one skilled in the art could make and use the claimed invention without undue experimentation.

In light of the above, Applicants submit that the present claims satisfy the requirements of 35 U.S.C. §112, first paragraph and respectfully request that the rejections be withdrawn.

VI. Claim Rejections Under 35 U.S.C. § 102

Claims 1 and 4 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Kingsman et al. (PCT Publication No. WO 03/089649).

Claims 1-4 and 6 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Fayen et al. (Methods in Enzymology, 2000, 327:351-368).

A. The Present Claims

Independent claim 1 is directed to a method of generating tethered extracellualar domains of transmembrane proteins. The method comprises preparing an expression vector comprising a 5' nucleic acid sequence encoding a signal polypeptide sequence, a nucleic acid encoding a purification epitope tag polypeptide, a sequence coding for an extracellular domain of a membrane protein, and a 3' nucleic acid encoding an anchor polypeptide sequence. Mammalian cells are transfected with the expression vector to generate an anchor tethered protein targeted to an extracellular domain of a plasma membrane. The anchor tethered protein is displayed on a lipid bilayer array or purified and reconstituted in membranes for display on a lipid bilayer array.

B. The Cited Art

Kingsman et al. relate to an expression vector comprising an amino-terminal tag sequence and a signal sequence operably linked to a nucleotide of interest (Abstract). The amino-terminal tag sequence is inserted between the signal sequence and the nucleotide sequence of interest (page 1, lines 7-9). The utility of the nucleotide sequence of interest is determined by transfecting a host cell with the expression vector, selecting for host cells expression the sequence, and determining the expression profile of the protein expressed from the nucleotide sequence of interest (page 4, lines 20-25). The expression profile of the protein can be used to determine whether the nucleotide sequence of interest is a disease target for use in cancer immunotherapy (page 3, lines 29-31). The nucleotide sequence is preferably a tumor associated antigen.

Fayen et al. describe engineering proteins bearing C-terminal GPI anchors in place of their normal transmembrane and intracellular sequences for incorporation into cell surface membranes (page 353, lines 4-6 and 16-18). Cells may be transfected with the cDNA encoding the GPI-modified protein and the modified protein (page 360, lines 3-5. The cDNA may be ligated into an expression vector (page 362, lines 6-7). The GPI-modified protein may be purified and incorporated into cells.

C. Analysis

The standard for lack of novelty, that is, for anticipation, is one of strict identity. To anticipate a claim for a patent, a single prior source must contain all its essential elements. M.P.E.P. § 2131.

Kingsman et al. and Fayen et al. each fail to teach at least a method including the step of *displaying the anchor tethered protein on a lipid bilayer array or purifying and reconstituting the anchor tethered protein in membranes for displaying on a lipid bilayer array*. Kingsman et al. teach their method may be used for screening using phage display techniques or transformed host cells (pages 56-57). Fayen et al. teach anchoring GPI-anchored proteins into cells (page 353, lines 7-8 and page 361, lines 19-22).

As neither Kingsman et al. nor Fayen et al. teach each and every element of the claimed method, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. §102.

VII. Conclusion

Applicants believe that the pending claims are in condition for Allowance. A Notice of Allowance is therefore respectfully requested.

If the Examiner has any questions or believes a telephone conference would expedite prosecution of this application, the Examiner is encouraged to call the undersigned at 650-590-1939.

The Commissioner is hereby authorized to charge any additional fees deemed to be due with the filing of this communication to Deposit Account No. 50-4616.

Respectfully submitted,

King & Spalding LLP

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